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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

July 13, 1973

RR-00785-01A1

Dr. Joshua Lederberg
Professor of Genetics
Stanford University
Stanford, California 94305

Dear Dr. Lederberg:

The National Advisory Research Resources Council (NARRC) concurred with the initial review group recommendation that your application, RR-00785, be approved with reduced budget.

The following quotes represent their impressions of the weak points of your application.

> "The utility of DENDRAL does not appear to lie in its contribution to MS within the foreseeable future . . . . Other instrumentation using GC/MS and library look-up or computer matching of spectra . . . is efficient, reliable, far less expensive, and less involved than the proposed method . . . .
>
> "Of the total range, three sub-projects of DENDRAL are neither good chemistry nor good computer science. Real-time computer control of MS may be feasible given that the computer programs have been established, but this portion of the proposal does not contribute to the basic investigation. Similarly, C^{13}-NMR has such low sensitivity that it requires 5-6 orders of magnitude more per sample than MS--and it contributes little to AI. Finally, the second part of B, the analysis of urinary metabolites, which is primarily of clinical interest, would be more simply done by library look-up of spectra of known, normal, and abnormal constituents of body fluids. Such a compendium has been compiled by Dr. Markey of the University of Colorado."

From a minority opinion favoring disapproval came the following notions:

> I have repeatedly requested enlightenment on why very large and expensive facilities are requested and how it may ultimately contribute to an understanding which would result in better medical care . . . . My feelings are that funding such large projects, of low payoff probability, could only result in positive harm to the total biomedical community . . . .

The reviewers reinforced the shared resource concept by stating:

> "In many ways the most significant aspect of the proposal is that an AI network resource would provide an excellent demonstration of resource sharing which would give that concept a maximum chance of success."

The budgets and rationale recommended are as follows:

BUDGET: SUMEX and DENDRAL:

Figure 1

SUMEX

SUMEX	-01	-02	-03	-04	-05
Personnel	$220,000	231,000+	242,500+	255,000+	267,500+
Equipment	175,000	175,000	175,000	175,000	175,000
Supplies	20,000	22,000	24,000	26,000	26,000
Communications	28,000	29,000	30,000	31,000	32,000
Other Expenses					
Maintenance	60,000	60,000	60,000	60,000	60,000
Freight	12,000	0	0	0	0
Miscellaneous	3,000	3,000	3,000	3,000	3,000
Travel	5,000	5,000	5,000	5,000	5,000
	$533,000	525,000	539,500	555,000	568,500
DENDRAL	*39,000	134,000	128,300	134,700	141,500
TOTAL	$572,000	659,000	667,800	689,700	710,000

*This is only four months for DENDRAL; the other eight months are the end of the previous grant period.

SUMEX Rationale:

1. Personnel: Funds cover the following positions (see p. 88 of SUMEX proposal for original request):

SUMEX facility head	1	(Rindfleish)
Network coordinator	1	(Jamtgaard)
Systems programmers	3	
Engineer	1	
Operators	3	
Application programmers	2	
Technicians	1	
Secretary	1	

2. Equipment: The equipment is such as to provide DENDRAL with the capability for Parts A (minus the C^{13}-NMR project) and C. Part B, the real-time control of MS and the use of DENDRAL to analyze urinary metabolites, was felt not to contribute to the major objectives of the AI program. The Bare system plus TIP was increased to $175,000 to allow for inexpensive terminals and the like.

3. Supplies: "Communication" is essentially as requested. Other supplies are cut by $20,000/year--deleting part of the engineering and the lab supplies. This is in line with not supporting the on-line DENDRAL work or GC/MS clinical projects.

4. Travel: Travel is reduced somewhat.

5. Other Expenses: "Maintenance" is recommended as requested and may possibly be somewhat higher than is really needed. It is assumed that BRB will monitor these expenses as well as the hardware purchases to ensure economy. Funds for purchasing computer time "terminal and computer services" have been deleted. "Other" has been slightly reduced. "Freight" is as requested.

DENDRAL

(Parts A & C only. Personnel projected from first year.)

	-01	-02	-03	-04	-05
Personnel	$36,800	116,000	122,000	128,000	134,500
Equipment	0	12,000	0	0	0
Supplies	700	2,000	2,100	2,200	2,200
Travel	0	1,000	1,000	1,000	1,000
Other	1,500	3,000	3,200	3,500	3,800
Terminals					
Telephone					
	+$39,000	134,000	128,300	134,700	141,500

+This is for a four-month period.

DENDRAL Rationale: Completion of Parts A and C should enable you to exploit fully the DENDRAL work. Figure 2 shows the recommended total budget. The personnel figure is derived from the first year request--multiplied by 3 and with 5% increment in each year. The equipment budget is for a graphics terminal. Two are requested, one is recommended. The other reductions are trivial except for travel. Total travel funds as given in the combined budgets seem adequate for a project of this size.

The issues still at large with this application require personal interaction to resolve them. The date of August 2, proposed by Tom Rindfleish, is satisfactory with Dr. Raub and me for a meeting at Stanford.

Hopefully, we can negotiate SUMEX to our mutual satisfaction and a fundable conclusion and lay out a pathway for DENDRAL that results in a MS resource diffusing its gains to its own disciplinary community as well as clinical research.

Sincerely yours,

William Roy Baker, Jr.

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